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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,364	10/06/2005	Lawrence C. Tisi	GRT/292-97	1155

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EXAMINER	
BAUGHMAN, MOLLY E	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,364	TISI ET AL.	
	Examiner	Art Unit	
	Molly E. Baughman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *34-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/6/05; 10/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-33) in the reply filed on 2/16/2007 is acknowledged. The traversal is on the ground(s) that the kit and apparatus of Groups II and III are specifically designed for carrying out the method of Group I. This is not found persuasive because the method of Group I *comprises* bringing into association the components necessary for nucleic acid amplification and a bioluminescence assay which are also present in the kit of Invention, however, the method could also entail bringing other components into association, such as Apyrase, or bringing in different polymerases, luciferases, primers, etc., as well as different concentrations of such components than those present in the kit of Group II. The kit of Group II could also be used in different methods than that of Group I, such as a sequencing reaction where the dNTPs are sequentially added. The apparatus of Group III could also be used in any bioluminescence reaction, comprising additional components and different steps than that of Group I. Group I could also use a different apparatus than that of Group III. Furthermore, the kit of Group II does not provide contribution over the prior art. Kits comprising a polymerase, substrates for nucleic acid polymerase, at least two primers, a thermostable luciferase, and luciferin were known in the prior art (see US 2003/0165861 A1, Wakabayashi et al., columns 3-4 [0037-0042]).

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 34-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or

linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/16/2007.

Information Disclosure Statement

3. The information disclosure statement filed 7/6/2005 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because there are no copies of each cited foreign patent document, and each non-patent literature publication. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

a. Specific items not found have been lined through (both WO documents, as well as all non-patent literature documents).

b. The International Search Report and Preliminary Examination Reports have been considered, although, they have been lined through as they are not appropriate documents for printed patents.

4. It is also noted that the foreign patent document, WO 2003/087388 A3 (03/2004), on Information Disclosure Statement filed 10/6/2005 has been considered, although, it

has been lined through since it is also an International Search Report document, inappropriate for printed patents.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

c. Claims 1-33 are confusing because it cannot be determined how a bioluminescence assay is able to occur when ATP sulphurylase and adenosine 5'-phosphosulphate are *optionally included* in claim 1 and they are required for the conversion of PPi to ATP, wherein ATP is required for luciferase to create light in the presence of luciferin. While claims 2-33 do not particularly recite the limitation, they depend from claim 1 which recites the limitation.

d. Claim 1 recites the limitation "the bioluminescence reaction." There is insufficient antecedent basis for this limitation in the claim. The claim refers to components necessary for a bioluminescence assay and a nucleic acid amplification reaction, however it does not refer to a bioluminescence reaction and there are no steps that correspond to such a reaction.

e. Claims 1-33 are confusing because it cannot be determined what is encompassed by “a bioluminescence assay,” and the specification refers to

numerous alternatives for such an assay. As such, it renders the method of claims 1-33 unclear. While claims 2-33 do not particularly use the term, they depend from claims which use the term.

f. Claims 6-7, 15, 17-18, and 28-33 are confusing because it is unclear how claims 6-7,15 and 28-33 are further limiting. The claims only recite intended uses, and it is unclear what further active steps are required. While claims 17-18 are further limiting, they depend from claim 15.

g. Claims 10-11, 18, and 21 are confusing because it cannot be determined how a decrease in the intensity of light output can occur in the method of claim 1. It would appear that in the method as stated in Claim 1, the pyrophosphate production would remain constant in an amplification reaction, and therefore the production of ATP by ATP sulphurylase, and consequently intensity of light output produced by luciferase via ATP would remain constant as well once reaching maximum. Clarification is required.

h. Claim 16 recites the limitation "whether the template nucleic acid is present in the sample" in claim 14. There is insufficient antecedent basis for this limitation in the claim. While claims 17-19 do not particularly use the phrase, they depend from claims which use the phrase.

i. Claims 26-27 are confusing because it cannot be determined how the amplification reaction of ii) is carried out at more than one temperature in the method according to claim 23, wherein claim 23 requires the amplification reaction to be carried out isothermally.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-19, and 22-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Nygren et al., "Quantification of HIV-1 Using Multiple Quantitative Polymerase Chain Reaction Standards and Bioluminometric Detection," Analytical Biochemistry, 2001, Vol.288, pp.28-38.

Regarding Claims 1-3, Nygren et al. discuss a method wherein i) a nucleic acid polymerase, substrates for the nucleic acid polymerase, at least two primers, a thermostable luciferase, and luciferin are brought into association; ii) a nucleic acid amplification reaction of the target nucleic acid involving more than one cycle of amplification is performed; iii) the intensity of light output from the bioluminescence reaction is monitored; and iv) the amount of template nucleic acid present in the sample is determined (claim 1) (i.e. immobilized template/primers added to D-luciferin, DNA polymerase, APS, ATP sulfurylase, luciferase, each dNTP, and the reaction being

monitored by a luminometer every 1 min. – Bioluminometric Quantification of PCR Products, pg. 30). They also discuss the reaction wherein at least ii) and iii) are carried out in a sealed vessel (claim 2) (i.e. immobilized template/primer brought into association with all products necessary for amplification and bioluminescence reaction and monitored every 1 min. – Bioluminometric Quantification of PCR Products, pg.30), and the intensity of light output is monitored during the nucleic acid amplification reaction (claim 3) (i.e. Figure 4).

Regarding Claims 4-11, Nygren discusses a method wherein iii) includes producing a data set of intensity of light output as a function of time (claim 4) (i.e. Figures 3 and 4A). The amount of template nucleic acid present is determined by measuring the data set the time taken to reach a point at which the rate of change of intensity of light output changes significantly (claim 5); is determined by measuring the data set time taken to reach a point at which the intensity of light output begins to increase (claim 8); is at maximum (claim 9) (i.e. see Figure 3, and pg. 34 – "the ascending curve indicates the polymerase activity (in pmol of Ppi produced) and time elapsed is indicated," and pg. 29, 1st column, last sentence – inorganic pyrophosphate released is proportional to the amount of visible light detected by the luminometer, and "plateau phase" – pg. 31, 2nd column).

Regarding Claims 12, 15-19, Nygren discusses the method wherein the amount of template nucleic acid present is determined by measuring from the data set of time taken to reach a point at which the intensity of light output reaches or crosses a predetermined level (i.e. the luminescence output was calibrated by the addition of a

known amount of inorganic pyrphophate (PPi), pg. 30 - Bioluminometric Quantification of PCR Products and Figure 3).

Regarding Claim 13, Nygren et al. discuss using a thermostable luciferase brought into association with the sample in step I) which is a reversibly-inhibited luciferase (i.e. firefly luciferase (abstract), inherently a reversibly-inhibited luciferase).

Regarding Claim 14, Nygren discusses the method wherein iv) further comprises comparing the intensity of light output to the intensity of light output from a control in which the sample comprises a known amount of template nucleic acid (use of quantitative standards at various concentrations pPA, pPC, pPT, pPG, in comparison to the test sample proviral HIV-1 DNA – Quantification of HIV-1 MN Strain, pg. 35).

Regarding Claims 22-33, Nygren discusses the method wherein the nucleic acid amplification reaction of ii) is a low temperature amplification method in which the cycling temperature does not exceed 75°C (claim 22 and 24); is carried out isothermally (claim 23); is carried out at a constant temperature at which the components of the amplification reaction and the bioluminescence assay are stable (claim 25) (i.e. reaction was carried out at room temperature, and successful light output is indication the components are stable (pg. 30 - Bioluminometric Quantification of PCR Products and Figure 3).

It is noted that due to the indefiniteness of claims 6-7, 10-11, 15-19, and 26-33, as described above, it cannot be determined how the art differs from the instant claimed invention.

9. Claims 1-12, 15-20, and 22-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Nyren et al., "Detection of Single-Base Changes Using a Bioluminometric Primer Extension Assay," Analytical Biochemistry, 1997, Vol. 244, No.2, pp.367-373.

Regarding Claims 1-3, Nyren et al. discuss a method wherein i) a nucleic acid polymerase, substrates for the nucleic acid polymerase, at least two primers, a thermostable luciferase, and luciferin are brought into association; ii) a nucleic acid amplification reaction of the target nucleic acid involving more than one cycle of amplification is performed; iii) the intensity of light output from the bioluminescence reaction is monitored; and iv) the amount of template nucleic acid present in the sample is determined (claim 1) (i.e. continuous monitoring of organic pyrophosphate (PPi) released as a result of the specific activity of DNA polymerase using primers in Table 1, 4 dNTPs, thermostable luciferase, and luciferin – pg.367, 2nd column, last paragraph; and pg.368, Single-Base Change Detection). They also discuss the reaction wherein at least ii) and iii) are carried out in a sealed vessel (claim 2) (i.e. pg.368, Single-Base Change Detection), and the intensity of light output is monitored during the nucleic acid amplification reaction (claim 3) (i.e. pg.368, Single-Base Change Detection, and Figures 2-5).

Regarding Claims 4-11, Nyren discusses a method wherein iii) includes producing a data set of intensity of light output as a function of time (claim 4) (i.e. Figures 2-5). The amount of template nucleic acid present is determined by measuring the data set the time taken to reach a point at which the rate of change of intensity of light output changes significantly (claim 5); is determined by measuring the data set

time taken to reach a point at which the intensity of light output begins to increase (claim 8); is at maximum (claim 9) (i.e. see Figures 2-5, and pg. 371, Sensitivity – "initial rate," "upper limit," and "lower limit").

Regarding Claims 12, 15-19, Nyren discusses the method wherein the amount of template nucleic acid present is determined by measuring from the data set of time taken to reach a point at which the intensity of light output reaches or crosses a predetermined level (i.e. "the luminescence output was calibrated by the addition of a known amount of ATP or PPi," pg.368, Single-Base Change Detection).

Regarding Claims 22-33, Nyren discusses the method wherein the nucleic acid amplification reaction of ii) is a low temperature amplification method in which the cycling temperature does not exceed 75°C (claim 22 and 24); is carried out isothermally (claim 23); is carried out at a constant temperature at which the components of the amplification reaction and the bioluminescence assay are stable (claim 25) (i.e. reaction was carried out at room temperature, and successful light output is indication the components are stable (pg.368, Single-Base Change Detection and Figures 2-5).

It is noted that due to the indefiniteness of claims 6-7, 10-11, 15-19, and 26-33, as described above, it cannot be determined how the art differs from the instant claimed invention.

10. Claims 1-7, 10-22, and 26-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Murray et al. (US 2004/0185457 A1).

Regarding Claims 1-3, Murray et al. discuss a method wherein i) a nucleic acid polymerase, substrates for the nucleic acid polymerase, at least two primers, a

thermostable luciferase, and luciferin are brought into association; ii) a nucleic acid amplification reaction of the target nucleic acid involving more than one cycle of amplification is performed; iii) the intensity of light output from the bioluminescence reaction is monitored; and iv) the amount of template nucleic acid present in the sample is determined (claim 1) (i.e. template, primers 1 and 2, D-luciferin, DNA polymerase, APS, ATP sulfurylase, luciferase, each dNTP, and the reaction being monitored by a luminometer every 10 sec. – abstract, page 2, Examples 4-7). They also discuss the reaction wherein at least ii) and iii) are carried out in a sealed vessel (claim 2) (i.e. Examples 4-7), and the intensity of light output is monitored during the nucleic acid amplification reaction (claim 3) (i.e. Examples 4-7, abstract, Figures 1-2, and page 2, specifically [0027]).

Regarding Claims 4, 6-7, and 10-11, Murray discusses a method wherein iii) includes producing a data set of intensity of light output as a function of time (claim 4) (i.e. Figure 2, Example 6 – [0053-0054]).

Regarding Claims 12, 15-19, Murray discusses the method wherein the amount of template nucleic acid present is determined by measuring from the data set of time taken to reach a point at which the intensity of light output reaches or crosses a predetermined level (i.e. signal:background ratio, Example 7, Figure 3).

Regarding Claim 13, Murray et al. discuss using a thermostable luciferase brought into association with the sample in step I) which is a reversibly-inhibited luciferase (i.e. firefly luciferase (page 2, [0022], [0028], [0030]), inherently a reversibly-inhibited luciferase).

Regarding Claim 14, Murray discusses the method wherein iv) further comprises comparing the intensity of light output to the intensity of light output from a control in which the sample comprises a known amount of template nucleic acid (use of test plasmid at 0.5 ng/pg, Examples 2 and 7).

Regarding Claims 22, and 26-33, Murray discusses the method wherein the nucleic acid amplification reaction of ii) is a low temperature amplification method in which the cycling temperature does not exceed 75°C (claim 22); (i.e. reaction first heated to 95°C for 30 sec., then cycled according to the parameters in Example 2 – Examples 2-7).

It is noted that due to the indefiniteness of claims 6-7, 10-11, 15-19, and 26-33, as described above, it cannot be determined how the art differs from the instant claimed invention.

SUMMARY

11. No Claims are free of the prior art.

12. Nyren et al. (US 2004/0142330 A1) and Hassibi et al. (US 2004/0197793 A1 – priority date Oct.29, 2002) are noted as references of interest.

CONCLUSIONS

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Molly E. Baughman whose telephone number is 571-272-4434. The examiner can normally be reached on Monday-Friday 8-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Molly E Baughman
Examiner
Art Unit 1637

MEB 4/10/07

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

4/12/07